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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/619,898	07/14/2003	Rune Robert, Isak, Erik Frants	VEOC.003.02US	7453

31272 7590 03/06/2006

RAE-VENTER LAW GROUP, P.C.
P.O. BOX 1898
MONTEREY, CA 93942-1898

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 03/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/619,898	FRANTS ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-40 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-40 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-21, 29-33 and 38, drawn to an isolated nucleic acid encoding an alpha1 subunit of a P/Q-type gated calcium channel or a specific fragment or derivative or homolog of said calcium channel, a nucleic acid that is at least 70% identical to the sequence of SEQ ID Nos. 1-42, an expression vector comprising said nucleic acid, and a host cell containing said nucleic acid.

Group II, claim(s) 22-25, 27 and 28, drawn to a method of identifying a gene which encodes a P/Q-type gated calcium channel by using the nucleic acid of claim 1 or 20.

Group III, claim(s) 26-28, drawn to a method of distinguishing between alleles of a gene which encodes a P/Q-type gated calcium channel by using the nucleic acid or fragment in claim 20.

Group IV, claim(s) 30-33, 39 and 40, drawn to an animal or a non-human transgenic animal comprising the nucleic acid set forth above.

Group V, claim(s) 34, drawn to a method for screening for an agent for treating FHM, EA-2, SCA6, migraine or other neurological disorder by using animal.

Group VI, claim(s) 35, drawn to a protein or peptide encoded by the nucleic acid of claim 1.

Group VII, claim(s) 36 and 37, drawn to a natural or synthetic antibody against a protein or peptide according to claim 35, and a method for diagnosing FHM, EA-2, SCA6, migraine or other neurological disorder associated with cation channel dysfunction by using said antibody.

Claims 27 and 28 link to inventions II-III. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claims 4 and 16-18. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also M.E.P.. § 804.01.

The inventions listed as Groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The special technical feature for groups I-VII is an isolated nucleic acid encoding an alpha1 subunit of a P/Q-type gated calcium channel or a specific fragment or derivative or homolog of said calcium channel, or a nucleic acid that is at least 70% identical to the sequence of SEQ ID Nos. 1-42. Ellis et al., 1995, teaches a nucleotide sequence, N_Geneseq_36 Accession No. Q84659, which is 95.1% identical to base 142 to 244 of

SEQ ID No. 4, and said nucleotide sequence encodes a human neuronal calcium channel subunit 1A1. Since the nucleotide sequences of SEQ ID Nos. 1-42 are not disclosed in the foreign application Netherlands 96202707.4 filed 9-27-96, therefore, the priority date of said application is not granted. Ophoff, 1996, teaches a nucleotide sequence, GenEmbl Accession No. Z80116, which is 100% identical to the sequence of SEQ ID No. 3, and said nucleotide sequence encodes a P/Q type calcium channel. Thus, no special technical feature has been contributed over the prior art by the instant invention. Further, the methods described in groups II, III, V and VII are drawn to materially distinct methods which differ at least in objectives, method steps, reagents and/or dosages used, schedules used, response variables, and criteria for success. Nucleic acids, proteins, antibodies, and transgenic animals are drawn to compositions having different chemical structure, physical properties and biological function, and they are different products. Therefore, groups I-VII do not relate to a single general inventive concept under PCT Rule 13.1.

Upon election of a group, a further restriction is required as follows:

Since the SEQ ID Nos. 1-42 recited in the claims of the present application represent different DNA sequences having various mixture of exon and intron sequences. They lack common property or activity and the function and utility of the nucleotide sequence of each SEQ ID No would differ from each other, therefore, they represent different products. Thus, the SEQ ID Nos. 1-42 recited in the claims of the present application do not relate to a single general inventive concept. Applicant is required to elect a **single** SEQ ID No. for consideration by examiner.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

2. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Shin-Lin Chen, Ph.D.

S. Chen

SHIN-LIN CHEN
PRIMARY EXAMINER

Notice of References Cited	Application/Control No. 10/619,898	Applicant(s)/Patent Under Reexamination FRANTS ET AL.	
	Examiner Shin-Lin Chen	Art Unit 1632	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Ellis et al., 1995, N_Geneseq_36 Accession No. Q84659.
	V	Ophoff, 1996, GenEmbl Accession No. Z80116.
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

```
FT                   /*tag=  a
XX
PN   WO9504822-A.
XX
PD   16-FEB-1995.
XX
PF   11-AUG-1994;    94WO-US09230.
XX
PR   11-AUG-1993;    93US-0105536.
PR   05-NOV-1993;    93US-0149097.
XX
PA   (SALK ) SALK INST BIOTECHNOLOGY IND ASSOC.
XX
PI   Ellis SB,  Gillespie A,  Harpold MM,  Mccue AF,  Williams ME;
XX
DR   WPI; 1995-090900/12.
DR   P-PSDB; R71008.
XX
PT   DNA encoding human calcium channel sub-unit(s) - used for
PT   developing prods. for studying calcium channels, e.g. for
PT   obtaining agonists and antagonists
XX
PS   Claim 1; Page 190-201; 285pp; English.
XX
CC   The primary transceipt of the alpha 1A subunit gene is
CC   alternatively spliced to yield at least two variant mRNAs.
CC   One form, alpha 1A-1 is given in Q84659/R71007, and the other,
CC   alpha 1A-2 is given in Q84660/R71008. Alpha 1A-2 differs from
CC   alpha 1A-1 encoding sequence at the 3' end in that it lacks a
CC   5 nt. sequence. This deletion shifts the reading frame and
CC   introduces a translation termination codon resulting in an
CC   alpha 1A-2 coding sequence that encodes a shorter alpha 1A
CC   subunit than that encoded by alpha 1A-1. DNA doncding alpha
CC   1A subunits can be isolated using all or a portion of the DNA
CC   having sequence Q84661, Q85659 or Q84660 or DNA obtd. from
CC   the phage lysate of an E. coli host contg. DNA encoding an alpha
CC   1A subunit that has been deposited in the ATCC under accession
CC   no. 75293. The DNA is such a phage includes the DNA fragment
CC   having the sequence in Q84661 which selectively hybridises under
CC   conditions of high stringency to DNA encoding alpha 1A DNA but not
CC   to DNA encoding alpha 1B.
XX
SQ   Sequence 7791 BP; 1675 A; 2436 C; 2258 G; 1422 T; 0 other;

  Query Match             36.7%;  Score 95;  DB 16;  Length 7791;
  Best Local Similarity   95.1%;  Pred. No. 2.8e-20;
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Qy     202 tgcggccgctcaagctggtgtctggaatcccaagtgcgtgagt 244
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RESULT   4
Q84659
ID   Q84659 standard; DNA; 7808 BP.
XX
AC   Q84659;
XX
DT   01-DEC-1995  (first entry)
XX
DE   Human neuronal calcium channel subunit alpha 1A-1.
XX
KW   Calcium channel subunit; antagonist; agonist; diagnosis;
KW   Lambert Eaton Syndrome; ss.
XX
OS   Homo sapiens.
XX
```

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FT   misc_difference 7035..7039
FT                   /*tag=  b
FT                   /note= "not present in alpha 1A-2"
XX
PN   WO9504822-A.
XX
PD   16-FEB-1995.
XX
PF   11-AUG-1994;    94WO-US09230.
XX
PR   11-AUG-1993;    93US-0105536.
PR   05-NOV-1993;    93US-0149097.
XX
PA   (SALK ) SALK INST BIOTECHNOLOGY IND ASSOC.
XX
PI   Ellis SB,  Gillespie A,  Harpold MM,  Mccue AF,  Williams ME;
XX
DR   WPI; 1995-090900/12.
DR   P-PSDB; R71007.
XX
PT   DNA encoding human calcium channel sub-unit(s) - used for
PT   developing prods. for studying calcium channels, e.g. for
PT   obtaining agonists and antagonists
XX
PS   Claim 1; Page 178-190; 285pp; English.
XX
CC   The primary transceipt of the alpha 1A subunit gene is
CC   alternatively spliced to yield at least two variant mRNAs.
CC   One form, alpha 1A-1 is given in Q84659/R71007, and the other,
CC   alpha 1A-2 is given in Q84660/R71008. Alpha 1A-2 differs from
CC   alpha 1A-1 encoding sequence at the 3' end in that it lacks a
CC   5 nt. sequence. This deletion shifts the reading frame and
CC   introduces a translation termination codon resulting in an
CC   alpha 1A-2 coding sequence that encodes a shorter alpha 1A
CC   subunit than that encoded by alpha 1A-1. DNA doncding alpha
CC   1A subunits can be isolated using all or a portion of the DNA
CC   having sequence Q84661, Q85659 or Q84660 or DNA obtd. from
CC   the phage lysate of an E. coli host contg. DNA encoding an alpha
CC   1A subunit that has been deposited in the ATCC under accession
CC   no. 75293. The DNA is such a phage includes the DNA fragment
CC   having the sequence in Q84661 which selectively hybridises under
CC   conditions of high stringency to DNA encoding alpha 1A DNA but not
CC   to DNA encoding alpha 1B.
XX
SQ   Sequence 7808 BP; 1680 A; 2441 C; 2265 G; 1422 T; 0 other;

  Query Match             36.7%;  Score 95;  DB 16;  Length 7808;
  Best Local Similarity   95.1%;  Pred. No. 2.8e-20;
  Matches   98;  Conservative    0;  Mismatches    5;  Indels    0;  Gaps    0;

Qy     142 gcatcttggcgacagttgggacggagtttgacctacggacgctgagggcagttcgagtgc 201
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Qy     202 tgcggccgctcaagctggtgtctggaatcccaagtgcgtgagt 244
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AC   Q29273;
XX
DT   03-MAR-1993  (first entry)
XX
DE   Human calcium channel 27980/15.
XX
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23	104.6	23.7	6984	11	AF042317	AF042317 Mus muscu
24	104.6	23.7	9695	11	AF055477	AF055477 Rattus no
25	104.2	23.6	7121	3	AF173882	AF173882 Bos tauru
26	103	23.4	7011	11	RATRBBI	M92905 Rat calcium
27	103	23.4	7185	11	MMU04999	U04999 Mus musculu
28	100	22.7	121866	84	HSJ322E17	AL109937 Homo sapi
29	99.6	22.6	2163	37	AF239258S1	AF239258 Homo sapi
c 30	99.6	22.6	150149	67	AL160059	AL160059 Homo sapi
31	98.2	22.3	2470	81	I12881	I12881 Sequence 14
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34	98.2	22.3	7175	81	AR063883	AR063883 Sequence
35	98.2	22.3	7175	81	AR067883	AR067883 Sequence
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37	98.2	22.3	7362	81	AR022379	AR022379 Sequence
38	98.2	22.3	7362	81	AR063882	AR063882 Sequence
39	98.2	22.3	7362	81	AR067882	AR067882 Sequence
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41	97	22.0	7713	3	RABBCCBIII	D14157 Rabbit mRNA
42	94.6	21.5	7792	3	OCBCCBII	X67856 O.cuniculus
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44	94.6	21.5	7892	4	AF173014	AF173014 Gallus ga
45	94.6	21.5	7920	4	AF173019	AF173019 Gallus ga

ALIGNMENTS

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RESULT   1
HSCAC3
LOCUS       HSCAC3          441 bp    DNA                 PRI       01-NOV-1996
DEFINITION  H.sapiens CACNL1A4 gene, exon 3.
ACCESSION   Z80116
VERSION     Z80116.1  GI:1657289
KEYWORDS    alpha1 subunit; CACNL1A4; calcium channel; P/Q type.
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Vertebrata; Mammalia; Eutheria;
            Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 441)
  AUTHORS   Ophoff,R.A.
  TITLE     Direct Submission
  JOURNAL   Submitted (09-SEP-1996) R.A. Ophoff, Leiden University, Human
            Genetics, Sylvius Laboratory, P.O. Box 9503, 2300 RA Leiden,
            NETHERLANDS
REFERENCE   2  (bases 1 to 441)
  AUTHORS   Ophoff,R.
  JOURNAL   Unpublished
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                     /db_xref="taxon:9606"
                     /map="19p13.1"
     gene            58. .197
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                     /usedin=Z80114:cac_mrna
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           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy      61 gacacagaaccatacttcattggaatttttttgtttcgaggctggaattaaaatcattgcc 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 GACACAGAACCATACTTCATTGGAATTTTTTGTTTCGAGGCTGGAATTAAAATCATTGCC 120

Qy     121 cttgggtttgccttccacaaaggctcctacttgaggaatggctggaatgtcatggacttt 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy     301 ttctccctccccttgttatgcgcctgcctcctttctgccaacaccccacctccatgtctc 360
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Db     361 AGCTGTATATTACAGCAGATGCTTTCTGTTACAATTAAAATAATAGCTCATTATTGTTGG 420

Qy     421 ctgcttccagagtgctttatg 441
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Db     421 CTGCTTCCAGAGTGCTTTATG 441


RESULT   2
A70682
LOCUS       A70682          441 bp    DNA                 PAT       07-MAY-1999
DEFINITION  Sequence 3 from Patent WO9813490.
ACCESSION   A70682
VERSION     A70682.1  GI:4774686
KEYWORDS    .
SOURCE      unidentified.
  ORGANISM  unidentified
            unclassified.
REFERENCE   1  (bases 1 to 441)
  AUTHORS   Ophoff,R.A., Terwindt,G.M., Ferrari,M.D. and Frants,R.R.
  TITLE     A gene related to migraine in man
  JOURNAL   Patent: WO 9813490-A 02-APR-1998;
            OPHOFF ROEL ANDRE (NL)
FEATURES             Location/Qualifiers
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                     /organism="unidentified"
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BASE COUNT       89 a    110 c    104 g    138 t
ORIGIN

  Query Match           100.0%;  Score 441;  DB 81;  Length 441;
  Best Local Similarity  100.0%;  Pred. No. 1.5e-131;
  Matches  441;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 gatcttgtcaacatctgcccagcccaagacgctgaccttgccttctctccccttccaggat 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy      61 gacacagaaccatacttcattggaatttttttgtttcgaggctggaattaaaatcattgcc 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 GACACAGAACCATACTTCATTGGAATTTTTTGTTTCGAGGCTGGAATTAAAATCATTGCC 120

Qy     121 cttgggtttgccttccacaaaggctcctacttgaggaatggctggaatgtcatggacttt 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 CTTGGGTTTGCCTTCCACAAAGGCTCCTACTTGAGGAATGGCTGGAATGTCATGGACTTT 180

Qy     181 gtggtggtgctaacggggtaagtggcgcgtgctatacgctttggatttaactagctgaag 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 GTGGTGGTGCTAACGGGGTAAGTGGCGCGTGCTATACGCTTTGGATTTAACTAGCTGAAG 240

Qy     241 gattacgaggcttttggttggtgtggtccgggccaggctcaggaaggctgagcccttgtg 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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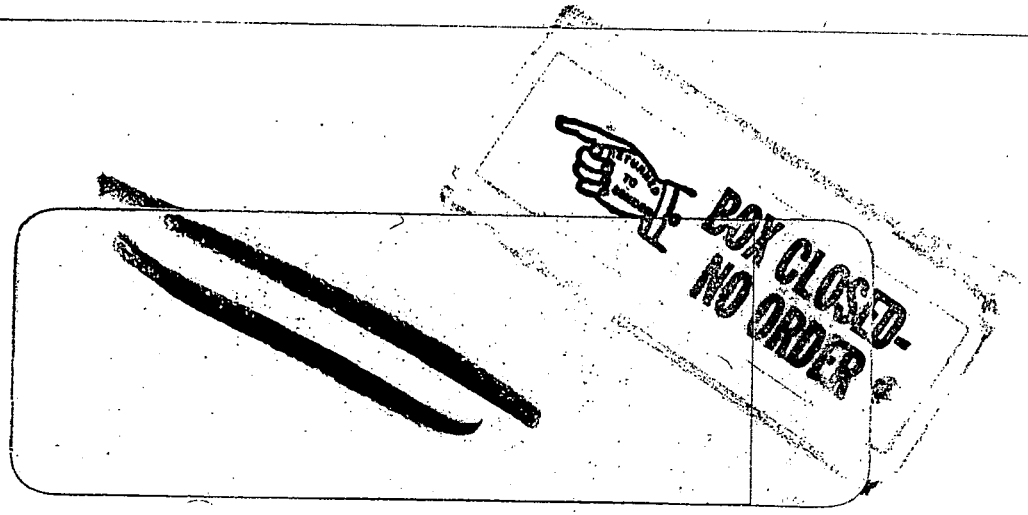

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Moved, Left No Address
Forwarding Order Expired
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